PCT/GB98/03137

- 1 - 422 Rec'd PCT/PTO 1 8 APR 2000

CONTROLLING HOUSE DUST MITES AND BEDMITES

Field of

This invention relates to methods of controlling house dust mites and bedmites (hereinafter HDM). HDM are typically 5 Dermatophagoides spp., one species οf particular significance being <u>D. pteronyssinus</u>.

A major food source for HDM is dead skin fragments (dander). Such fragments are continually shed by humans in considerable quantities. HDM proliferate in particular in 10 bedding, including the fillings of pillows and mattresses, and in upholstered articles and fibrous floor coverings. HDM are xerophilic organisms which do not require liquid water, and they live in the absence thereof. They demand a high humidity environment, requiring a relative humidity (R.H.) 15 of about 70 to 80 percent to survive. They absorb little water from the atmosphere and are effectively reliant on their food as the source of water. HDM typically excrete about 20 dung pellets per day. These pellets are very dry and brittle and are about 30 micron in size. They are 20 readily broken up into particles about 1-10 micron in size. In the absence of free moisture, these particles readily acquire a positive static charge and become airborne. are of respirable size and are accordingly able to enter the bronchial tubes of the human lung, where they become 25 deposited on the mucus layer in the tubes and absorb water. The particles contain toxins, which are released when the particle is hydrated, and they can cause rapid allergic reactions, including bronchial inflammation and asthmatic symptoms. One such allergenic toxin of major importance is 30 Der p I, which is a highly-stable water-soluble glycopeptide of molecular weight 30,000 derived from the digestive system of <u>D. pteronyssinus</u>.

Considerable effort has been expended in devising methods for controlling allergic reactions caused by the 35 presence of HDM. One general method is the topical use of

acaricides (the generic name for substances lethal to mites). Other methods rely upon control of the allergenic particles, for example by encasing them or by denaturing or destroying the allergens they contain. A further method 5 relies on the topical application of fungicides. Dead skin fragments as shed have a very low moisture content and a high fat content. As such, they are a poor food source for Furthermore, HDM require a source of 3-group vitamins. Certain microscopic fungi which thrive in the 10 absence of liquid water (xerophilic fungi) grow on dead skin fragments, and they have the ability to absorb moisture from the atmosphere. In consequence, the moisture content of the fragments is raised; their fat content is reduced; and furthermore B-group vitamins and ergosterol, a precursor of 15 vitamin D, are generated. All this makes the fragments a more suitable food source for HDM. Many such fungi belong to the Aspergillus glaucus and A. restrictus groups. Particular species include A. penicilloides and Eurotium repens (A. repens).

It is believed that <u>Aspergillus spp.</u> such as <u>A. repens</u> and <u>A. penicilloides</u> are not responsible per se for allergic reactions in humans of the kind induced by HDM.

Topical application of fungicides has the disadvantage that repeated treatment at regular intervals is required for 25 continued control of HDM. Furthermore, fungicides are inherently toxic materials, and domestic topical application of such substances has been criticised for that reason. It is an object of the invention to provide a means of overcoming these disadvantages.

30 Disclosure of the invention

According to the invention, there is provided in a first aspect the use of a polymeric article having incorporated therein a chemical compound which has antifungal activity against fungi of the groups <u>Aspergillus</u> 35 <u>glaucus</u> and/or <u>A. restrictus</u> as a means of controlling HDM.

Particular species of such fungi include \underline{A} . $\underline{penicilloides}$ and \underline{A} . \underline{repens} . A particular species of \underline{HDM} is \underline{D} . $\underline{pteronyssinus}$. The chemical compound may exhibit fungicidal and/or fungistatic activity.

The polymeric article may be a natural article, for . 5 example a cellulosic fibre, into which the chemical compound has been incorporated by, for example, a dyeing process. Alternatively, which may be preferred, the polymeric article may be a manmade article such as a fibre or foam into which 10 the chemical compound has been incorporated by a dyeing process or, more preferably, during the course of its manufacture. In the case of a fibre, such a manmade article may be of a natural polymer such as cellulose or of a synthetic polymer such as an acrylic polymer based on 15 polyacrylonitrile. Manmade fibres are described, example, in a series of articles entitled "Fibers" in Ullmann's Encyclopaedia of Industrial Chemistry, 5th edition (VCH Publishing), Vol. A10 (1987) and A11 (1988). case of a foam, the manmade article may be of a synthetic 20 polymer such as a polyurethane. Fibres are used for the manufacture of textile articles such as bedding fabrics (including sheets, blankets, pillowcases, mattress covers and the like), upholstery fabrics and floor coverings Both fibres and foams are used as filling 25 materials in articles such as pillows, mattresses, duvets and cushions, in which dander may accumulate and HDM thrive. Foams are used as backing materials and underlays for carpets.

According to the invention there is provided in a second aspect a filling material for an article of bedding or an upholstered article, characterised in that in said filling material is incorporated a chemical compound which exhibits antifungal activity against fungi of the groups Aspergillus glaucus and/or A. restrictus. The filling material is preferably in fibrous form. The invention further provides an article of bedding or an upholstered article filled with such material. The invention further

provides a carpeting material which includes a fibre or foam incorporating such a chemical compound.

Insects such as HDM and mammals such as humans on the one hand and fungi such as Aspergillus spp. on the other 5 hand belong to different taxonomic kingdoms. Many substances are known which are toxic to organisms within one kingdom but are effectively non-toxic to organisms within other kingdoms. The same is true, although to increasingly lesser degrees, between the lower taxonomic divisions 10 beginning with phyla, classes and orders. It is an advantage of the invention that it can make use of antifungal compounds having low toxicity to higher mammals including humans and domestic animals and to other domestic pet creatures. The use of such compounds is accordingly 15 preferred.

fibres which incorporate neutral organic compounds such as tolnaftate (which fungicidal preferred compound), bifonazole, clotrimazole, miconazole, dichlorophene or hexachlorophene are disclosed 20 GB-A-2,309,461, and these fibres may be preferred in the invention. Another suitable compound is triclosan. amount of the fungicidal compound in such fibres preferably in the range from 0.01 to 2 percent by weight on the weight of fibre. Similar amounts of such fungicidal 25 compounds are suitable also in other kinds of polymeric article of the invention.

Incorporation of the antifungal compound within the polymeric article has the advantages that release of the 30 compound into the environment is minimised and that the antifungal effect is long-lasting and endures throughout laundering and dry-cleaning. Wet-spun acrylic fibres may have the advantage of a fissured structure, which both confers good moisture transport properties and assists 35 diffusion of the antifungal compound to the fibre surface following depletion therefrom. The low moisture regain of synthetic fibres such as acrylic fibres may also be

advantageous in maintaining a low humidity environment and thereby interfering with growth of <u>Aspergillus spp.</u> and HDM.

The invention is illustrated by the following Example, in which parts and proportions are by weight unless 5 otherwise specified:-

Example

This Example illustrates the fungicidal activity against <u>A. repens</u> of acrylic fibres which incorporate a fungicide and of the use of such fibres in controlling HDM.

Acrylic fibres containing 0.4% tolnaftate were prepared by a similar method to that disclosed in Example 1 of GB-A-2,309,461. Such fibres are available commercially from Courtaulds Fibres (Holdings) Limited under the Trade Mark AMICOR AF. Acrylic fibres containing no antifungal agent 15 (available from Courtaulds Fibres (Holdings) Limited under the Trade Mark COURTELLE) were used as control. antimicrobial activity of the fibres was measured by the streak method disclosed in Example GB-A-2,309,461, but using a culture of A. repens (IMI 20 094150) containing ca. 3x10° spores/ml. Test plates were incubated at 25°C for 4 days. The widths of inhibition fyngal growth were measured, and the results zones of range and in parenthesis the average of 12 measurements) are reported in the Table below:

WO 99/21421 PCT/GB98/03137

- 6 -

Table 1

Width of inhibition zone

Control	Confluent growth in all	streaks on all plates
	Minimum mm	Maximum mm
5 Fibre with tolnaftate	G-2 (0.7)	2-6 (3.9)

Human skin (provided by a chiropodist) was sterilised. ground into fine fragments and wetted with synthetic perspiration. It was then used as a culture medium for A. repens. A needle punched nonwoven fabric of open structure 10 was placed in a deep glass dish, to which was then added a known amount of the A. repens culture and fifty HDM. Sticky tape was affixed to the upper part of the dish wall to entrap HDM attempting to climb the wall. The dish was then cultured for eight weeks at room temperature and 75% R.H. 15 The number of HDM stuck to the tape was recorded. associated with the fabric were driven out by application of heat, and their number was recorded. The results shown in Table 2 were obtained (average of three cultures in each case).

20 Table 2

	Fabric	HDM OI	n tape	HDM w	ith fabric	Total
	Amicor AF .		36.6		16.0	42.6
	Amicor AB		21.7		1.3	23.0
	50/50 Amicor AF/Amicor	AB	11.3		2.3	13.6
25	Courtelle		32.3	-	46.0	78.3

AMICOR AB (Trade Mark of Courtaulds Fibres (Holdings) Limited) is an acrylic fibre containing triclosan made in similar manner to AMICOR AF.

The average number of HDM associated with the Amicor AF 30 fabric may be distorted by an apparent rogue result; the individual numbers recorded were 4, 9 and 35.

 If a large number of HDM is found associated with the fabric, the presence of HDM on the tape suggests a thriving culture which is attempting to colonise other areas. If a small number of HDM is found associated with the fabric, the 5 presence of HDM on the tape suggests an attempt by HDM to emigrate from a barren environment.

In comparative experiments, the same procedure was followed except that a synthetic food medium for HDM was used instead of the <u>A. repens</u> culture. HDM thrived on all the samples, 10 and there was no significant difference in HDM numbers between any of the samples.